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# GELLAN-GUM NANOPARTICLES AND METHODS OF MAKING AND USING THE SAME

## CROSS-REFERENCE TO RELATED APPLICATIONS

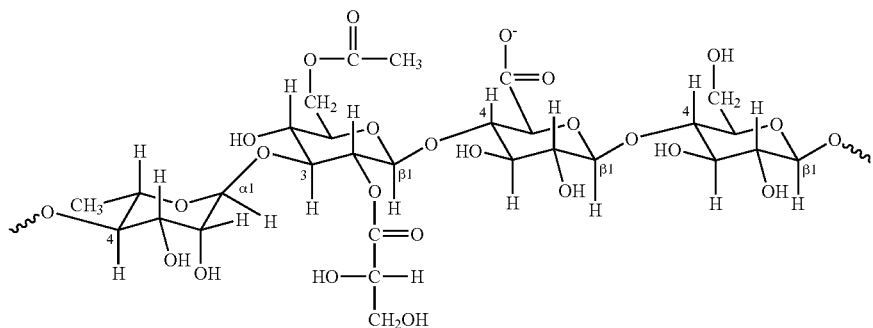
This patent application claims the benefit of priority to U.S. Provisional Patent Application Ser. No. 61/068,503 filed on Mar. 7, 2008 and entitled "GELLAN-GUM NANOPARTICLES AND METHODS OF MAKING AND USING THE SAME", the subject matter of which is hereby incorporated by reference in its entirety.

## TECHNICAL FIELD

The present invention relates to compositions containing a reaction product of gellan gum and polyethylene glycol (PEG). The present invention also relates to methods of making controlled-release gellan gum nanoparticles and methods of using controlled-release gellan gum nanoparticles, for example, as a drug delivery device.

## BACKGROUND

Gellan gum is an exocellular, microbial polysaccharide produced by *Pseudomonas elodea* and has been employed as a food additive. According to the FDA (21 CFR §172.665) gellan gum "may be safely used as a direct food additive for human consumption." The structural formula for gellan gum has been studied extensively and reported to consist of repeating tetrasaccharide units with the following structure:



which can also be represented by:

-3-β-D-glcp-(1-4)-β-D-glcpA-1-4)-β-D-glcp-(1-4)-α-L-rhamp-(1-

wherein "glcp" designates glucose, "glcpA" designates glucuronic acid, and "rhamp" designates rhamnose.

Gellan gum is commercially available in a clarified form under the trade designation KELCOGEL® for foods and industrial products and under the trade designation GELRITE® from CP Kelco, A Huber Company, (J.M. Huber Corporation, Edison, N.J.) for microbiological media, plant tissue culture, and pharmaceutical applications. Gellan gum has the potential to form gels in situ in the presence of mono- or divalent cations.

Gellan gum microparticles may be useful in encapsulating both bacteria and drugs (see, for example, U.S. Pat. Nos. 4,822,534 and 5,516,543). However, these gellan gum formulations of the prior art result in low biodistribution of encapsulated material, a feature attributed to susceptibility of the

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gellan gum polymer to degradation, which could present potential toxicity problems for applications such as anti-cancer drug delivery.

The physiological environment of tumors necessitates drug delivery systems that are capable of maintaining a controlled-release profile in acidic conditions. Thus, better formulations of gellan gum with improved controlled-release characteristics are needed for active drug targeting in vivo.

## SUMMARY

The present invention addresses some of the difficulties and problems discussed above by the discovery of gellan gum compositions suitable for use as a drug delivery host, wherein the compositions comprise a reaction product of gellan gum and polyethylene glycol (PEG). The gellan gum compositions may be complexed with a biologically active substance to form a drug delivery complex comprising, for example, nanoparticles of the reaction product of gellan gum and PEG and a biologically active substance. In one exemplary embodiment, the biologically active substance comprises an anti-carcinogenic compound.

Accordingly, in one exemplary embodiment, the present invention is directed to a composition comprising a reaction product of gellan gum and PEG. In one exemplary embodiment of the present invention, gellan gum is reacted with a functionalized polyethylene glycol having one or more terminal end groups comprising (i) an amine group, (ii) a carboxyl group, or both (i) and (ii) to form gellan gum derivatives that are more biologically compatible, and are capable of maintaining a controlled-release profile in acidic environ-

ments. The present invention also comprises of gellan gum-PEG complex nanoparticles with functionalized surface, whereby the surface functionalization is accomplished via ligand or protein attachment either covalently or otherwise. In one exemplary embodiment, a bifunctional ligand (e.g., RNA-aptamer ligand) is covalently bonded to surfaces of gellan gum-PEG nanoparticles so as to provide an enhanced affinity for a particular material (e.g., a protein).

The present invention is further directed to a method of making a biocompatible, biodegradable and water-soluble gellan gum derivative, wherein the method comprises covalently bonding gellan gum to PEG. In some exemplary embodiments, the covalently bonding step comprises reacting a carboxylic acid group of the gellan gum with a carbodiimide to form an amine reactive intermediate; and reacting the amine reactive intermediate with a functionalized PEG having a terminal amine end group. In other embodiments, the amine reactive intermediate may be reacted with a functionalized PEG having a terminal amine end group and a